

FIG. 1B. This array contains “spots” that each contain a single molecule, each corresponding to a molecule from single pathogen.

[0023] Locations on arrays may contain may also contain mixtures of molecules. Such mixtures may be derived from any number of sources. For example, locations on arrays may contain cell extracts, viral extracts, or molecules that are given off (e.g., molecules that may be obtained from culture media that has been in contact with pathogenic agents, such as a conditioned medium) by one or more pathogenic agents. Cell extracts may be prepared from cells that contain one or more molecules capable of binding at least one antibody produced in response to one or more pathogenic agent. As an example, a cell line may be constructed that expresses domains of two different proteins of a pathogenic agent. A cell extract, as well as other composition referred to above, may be prepared and used to generate a location on an array.

[0024] When a mixture of molecules is positioned in a spot, these molecules may be from the same pathogenic agent or from one or more pathogenic agents. Further, these mixtures of molecules may be prepared by combining purified (e.g., partially purified) molecules or by application to the array of a cell extract (e.g., a cell extract from cells infected with a single pathogenic agent or multiple different pathogenic agents). Such cell extracts may be prepared by introducing nucleic acids into the cells (e.g., by transfection, transduction, infection, etc.), followed by lysis of the cells. Further, cell extracts may be combined in a single spot (e.g., mixed before application to an array or spotted in the same location).

[0025] Locations on arrays may also contain vaccine compositions (with or without adjuvants being present). The presence of a vaccine composition on an array may be advantageous when one seeks to determine whether an immunological response has been directed against one or more of the vaccine's components. Thus, in this aspect, the invention is directed to methods and compositions for determining whether a particular vaccine has directed an immunological response to one or more component of the vaccine. Of course, the presence of such a response does not necessarily indicate the induction of protective immunity by the vaccine.

[0026] In addition to cell extracts, locations on arrays may contain one or more virus (e.g., heat killed virus). For example, array spots may contain two or more (e.g., two, three, four, five, etc.) related viruses (e.g., influenza viruses) that are different strains.

[0027] The invention also includes methods and compositions for characterizing host responses to pathogens, as well as nonpathogens. Such host responses may then be analyzed for any number of purposes. As an example, an organism's “fingerprint” may be identified. One type of fingerprint would be the induction of production of antibodies with specificity for particular proteins and/or regions of particular proteins. Fingerprints may be used to identify biomarkers, identify individuals with current exposure (e.g., infected individuals), or identify individual with past exposure to one or more organisms or interest (e.g., pathogens).

[0028] Along the lines of the above, the invention also provides methods and compositions for identifying pathogen molecules that are capable of inducing the production of antibodies that cross-react with host molecules. Thus, the invention also relates to the identification of molecules that

are capable of inducing, for example, autoimmune responses in individuals that harbor the organism.

BRIEF DESCRIPTION OF THE FIGURES

[0029] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

[0030] FIG. 1A and FIG. 1B. Exemplary compositions of the invention. FIG. 1A shows the composition, in this case a microarray, before contact with a sample. The twenty-four spots to the far left, in columns 1-4 (Section 1) and identified by vertically hatched circles, represent locations of proteins from different species and strains of *Mycobacteria*. The spots in columns 5-8 (Section 2) and identified by open circles represent the locations of proteins that are bound by antibodies generated in response to common vaccines. The spots in columns 9-10 (Section 3) and identified by stippled circles represent the locations of proteins that are bound by antibodies generated in response to immunodeficiency viruses such as HIV and HTLV. The twenty-four spots to the far right, in columns 11-14 (Section 4) and identified by horizontally hatched circles, represent locations of proteins from different species and strains of bacteria associated with sexually transmitted diseases (e.g., *Treponema pallidum*, *Chlamydia trachomatis*, human papilloma viruses, etc.). The bar code at the right can encode specific information, for example the individual being tested, the date, the test location, etc. FIG. 1B shows the same microarray after contact with a sample, with solid black circles representing “positives”.

[0031] FIG. 2A, FIG. 2B, and FIG. 2C. A schematic of methods of the invention as applied to vaccine development. In this embodiment, an immunological response induced by a known vaccine is compared to immunological responses induced by test vaccines. FIG. 2A represents an immunological response (“good” antibody profile) induced in humans by a known (licensed) vaccine. Historically, this vaccine was known to protect against smallpox in the years before smallpox was eradicated. FIG. 2B represents an immunological response (“good” antibody profile) induced in humans by a new vaccine that cannot be definitively tested for protection against human smallpox. FIG. 2C represents an immunological response (“poor” antibody profile) induced in humans by a new vaccine that is unlikely to fully protect.

[0032] FIG. 3. An “antibody fingerprint” for multiple pathogenic agents, in this example influenza A (row 1), influenza B (row 2), tularemia (row 3), SARS (row 4), avian flu (row 5), dengue (row 6), rubella (row 7), polio (row 8), and mumps (row 9). Positive reaction indicated by filled circles, intermediate reaction indicated by stippled circles, no reaction indicated by open circles.

[0033] FIG. 4A, FIG. 4B, and FIG. 4C. One use of arrays of the invention. In this embodiment, arrays are used to determine whether an individual is infected with a pathogen and, if so, what is the stage of infection. FIG. 4A represents the array profile of a healthy individual. FIG. 4B represents the array profile of a pre-symptomatic infected individual. FIG. 4C represents the array profile of an individual with early stage disease.

[0034] FIG. 5. One use of arrays of the invention. In this embodiment, arrays are used to determine whether an individual is infected with a pathogen and, if so, what specific